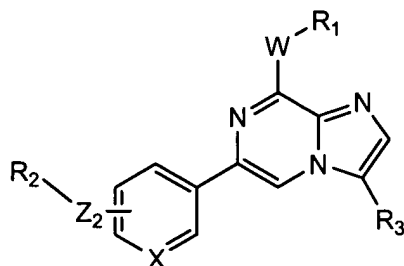


CLAIMS

What is claimed is:

1. A compound having Formula 1:



(Formula 1)

and the pharmaceutically-acceptable salts and prodrugs thereof, wherein:

R₁ is pyridyl or pyrimidinyl, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₇cycloalkyl, C₁-C₆alkoxy, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, C₁-C₆alkylthio, (C₁-C₆alkoxy)C₁-C₆alkyl, (C₁-C₆alkoxy)C₁-C₆alkoxy, mono- and di-(C₁-C₆alkyl)amino, amino(C₁-C₆alkyl), mono- and di-(C₁-C₆alkyl)amino(C₁-C₆alkyl), C₂-C₆alkanoyl, and -C(O)R₁₃ where R₁₃ is C₁-C₃haloalkyl, phenyl, heterocycloalkyl, or heteroaryl;

W is phenyl or a 5- or 6-membered heteroaryl containing from 1 to 4 heteroatoms independently chosen from nitrogen, oxygen, and sulfur; wherein W is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, oxo, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₇cycloalkyl, C₁-C₆alkoxy, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, (C₁-C₆alkoxy)C₁-C₆alkyl, (C₁-C₆alkoxy)C₁-C₆alkoxy, C₁-C₆alkylthio, mono- and di-(C₁-C₆alkyl)amino, amino(C₁-C₆alkyl), mono- and di-(C₁-C₆alkyl)amino(C₁-C₆alkyl), and C₂-C₆alkanoyl;

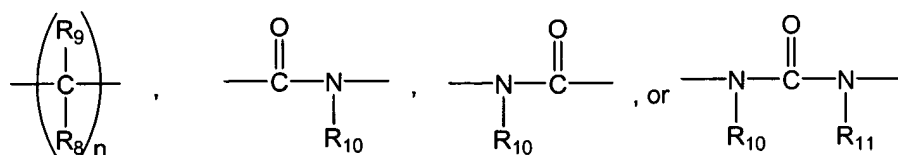
X is N or CH;

R₂ is C₁-C₇alkyl, C₃-C₇cycloalkyl(C₀-C₂alkyl), heterocycloalkyl(C₀-C₂alkyl), C₁-C₆alkoxy, (C₁-C₆alkoxy)C₁-C₆alkyl, or (C₁-C₆alkoxy)C₁-C₆alkoxy; or

R₂ is phenyl(C₀-C₂alkyl) or heteroaryl(C₀-C₂alkyl), each of which is substituted with 0 to 3 substituents independently chosen from

- (i) hydroxy, halogen, nitro, cyano, amino, sulfonamide, -CHO, C₁-C₆haloalkyl, and C₁-C₆haloalkoxy, and
- (ii) C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₇cycloalkyl, C₁-C₆alkoxy, (C₁-C₆alkoxy)C₁-C₆alkyl, (C₁-C₆alkoxy)C₁-C₆alkoxy, C₁-C₆alkylthio, mono- and di-(C₁-C₆alkyl)amino, amino(C₁-C₆alkyl), mono- and di-(C₁-C₆alkyl)amino(C₁-C₆alkyl), C₂-C₆alkanoyl, heterocycloalkyl(C₀-C₂alkyl), and -C(O)R₁₃; each of which (ii) is substituted with 0 to 3 substituents independently chosen from halogen, hydroxy, amino, nitro, cyano, C₁-C₄alkoxy, C₃-C₇cycloalkyl, and mono- and di-(C₁-C₄alkyl)amino;

Z₂ is



wherein

R₈ and R₉ are independently hydrogen, C₁-C₆alkyl, C₁-C₆alkoxy, or halogen; and n is 0, 1, or 2;

R₁₀ and R₁₁ are independently

(iii) hydrogen or C₁-C₆alkyl; or

(iv) phenyl or heteroaryl, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₇cycloalkyl, C₁-C₆alkoxy, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, (C₁-C₆alkoxy)C₁-C₆alkyl, (C₁-C₆alkoxy)C₁-C₆alkoxy, C₁-C₆alkylthio, mono- and di-(C₁-C₆alkyl)amino, amino(C₁-C₆alkyl), mono- and di-(C₁-C₆alkyl)amino(C₁-C₆alkyl), C₂-C₆alkanoyl, and -C(O)R₁₃;

R₃ is hydrogen or C₁-C₆alkyl, or

R₃ is C₃-C₇cycloalkyl(C₀-C₂alkyl), heterocycloalkyl(C₀-C₂alkyl), phenyl, or heteroaryl, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₇cycloalkyl, C₁-C₆alkoxy, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, (C₁-C₆alkoxy)C₁-C₆alkyl, (C₁-C₆alkoxy)C₁-C₆alkoxy, C₁-C₆alkylthio, mono- and di-(C₁-C₆alkyl)amino, amino(C₁-C₆alkyl), mono- and di-(C₁-C₆alkyl)amino(C₁-C₆alkyl), C₂-C₆alkanoyl, and -C(O)R₁₃; or

R₃ is phenoxy phenyl, each of which phenyl rings is substituted with 0 to 3 substituents

independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₇cycloalkyl, C₁-C₆alkoxy, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, (C₁-C₆alkoxy)C₁-C₆alkyl, (C₁-C₆alkoxy)C₁-C₆alkoxy, C₁-C₆alkylthio, mono- and di-(C₁-C₆alkyl)amino, amino(C₁-C₆alkyl), mono- and di-(C₁-C₆alkyl)amino(C₁-C₆alkyl), C₂-C₆alkanoyl, and -C(O)R₁₃.

2. A compound or salt according to Claim 1, wherein

R₁ is 3- or 4-pyridyl, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₇cycloalkyl, C₁-C₆alkoxy, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, (C₁-C₆alkoxy)C₁-C₆alkyl, (C₁-C₆alkoxy)C₁-C₆alkoxy, C₁-C₆alkylthio, mono- and di-(C₁-C₆alkyl)amino, amino(C₁-C₆alkyl), mono- and di-(C₁-C₆alkyl)amino(C₁-C₆alkyl), and C₂-C₆alkanoyl;

W is phenyl or a 5- or 6-membered heteroaryl ring; substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, oxo, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₇cycloalkyl, C₁-C₆alkoxy, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, (C₁-C₆alkoxy)C₁-C₆alkyl, (C₁-C₆alkoxy)C₁-C₆alkoxy, C₁-C₆alkylthio, mono- and di-(C₁-C₆alkyl)amino, amino(C₁-C₆alkyl), mono- and di-(C₁-C₆alkyl)amino(C₁-C₆alkyl), and C₂-C₆alkanoyl;

X is N or CH;

R₂ is C₁-C₇alkyl, C₃-C₇cycloalkyl(C₀-C₂alkyl), heterocycloalkyl(C₀-C₂alkyl), C₁-C₆alkoxy, (C₁-C₆alkoxy)C₁-C₆alkyl, or (C₁-C₆alkoxy)C₁-C₆alkoxy; or

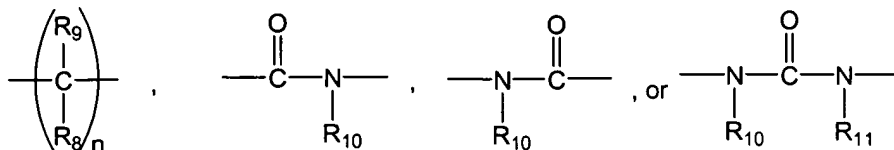
R₂ is phenyl(C₀-C₂alkyl) or 5- or 6-membered heteroaryl(C₀-C₂alkyl), each of which is substituted with 0 to 3 substituents independently chosen from

(i) hydroxy, halogen, nitro, cyano, amino, sulfonamide, -CHO, C₁-C₆haloalkyl, and C₁-C₆haloalkoxy, and

(ii) C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₇cycloalkyl, C₁-C₆alkoxy, (C₁-C₆alkoxy)C₁-C₆alkyl, (C₁-C₆alkoxy)C₁-C₆alkoxy, C₁-C₆alkylthio, mono- and di-(C₁-C₆alkyl)amino, amino(C₁-C₆alkyl), mono- and di-(C₁-C₆alkyl)amino(C₁-C₆alkyl), C₂-C₆alkanoyl, and heterocycloalkyl(C₀-C₂alkyl); each of which (ii) is substituted with 0 to 3

substituents independently chosen from halogen, hydroxy, amino, nitro, cyano, C₁-C₄alkoxy, C₃-C₇cycloalkyl, and mono- and di-(C₁-C₄alkyl)amino;

Z₂ is



wherein

R₈ and R₉ are independently hydrogen, C₁-C₆alkyl, C₁-C₆alkoxy, or halogen; and n is 0, 1, or 2;

R₁₀ and R₁₁ are independently

(iii) hydrogen or C₁-C₆alkyl; or

(iv) phenyl or a 5- or 6 membered heteroaryl ring, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₇cycloalkyl, C₁-C₆alkoxy, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, (C₁-C₆alkoxy)C₁-C₆alkyl, (C₁-C₆alkoxy)C₁-C₆alkoxy, C₁-C₆alkylthio, mono- and di-(C₁-C₆alkyl)amino, amino(C₁-C₆alkyl), mono- and di-(C₁-C₆alkyl)amino(C₁-C₆alkyl), and C₂-C₆alkanoyl;

R₃ is hydrogen or C₁-C₆alkyl, or

R₃ is C₃-C₇cycloalkyl(C₀-C₂alkyl), heterocycloalkyl(C₀-C₂alkyl), phenyl, or a 5- or 6-membered heteroaryl, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₇cycloalkyl, C₁-C₆alkoxy, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, (C₁-C₆alkoxy)C₁-C₆alkyl, (C₁-C₆alkoxy)C₁-C₆alkoxy, C₁-C₆alkylthio, mono- and di-(C₁-C₆alkyl)amino, amino(C₁-C₆alkyl), mono- and di-(C₁-C₆alkyl)amino(C₁-C₆alkyl), and C₂-C₆alkanoyl; or

R₃ is phenoxyphenyl, each of which phenyl rings is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₇cycloalkyl, C₁-C₆alkoxy, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, (C₁-C₆alkoxy)C₁-C₆alkyl, (C₁-C₆alkoxy)C₁-C₆alkoxy, C₁-C₆alkylthio,

mono- and di-(C₁-C₆alkyl)amino, amino(C₁-C₆alkyl), mono- and di-(C₁-C₆alkyl)amino(C₁-C₆alkyl), and C₂-C₆alkanoyl.

3. A compound or salt according to Claim 2 wherein

R₁ is 3-pyridyl or 4-pyridyl, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, halogen, C₁-C₆alkyl, C₃-C₇cycloalkyl, C₁-C₆alkoxy, C₁-C₂haloalkyl, C₁-C₂haloalkoxy, and mono- and di-(C₁-C₄alkyl)amino.

4. A compound or salt according to Claim 3 wherein

R₁ is 3-pyridyl or 4-pyridyl, each of which is substituted with 0 to 2 substituents independently chosen from fluoro, chloro, bromo, C₁-C₂alkyl, and C₁-C₂alkoxy.

5. A compound or salt according to any one of Claims 1 to 4 wherein

W is phenyl, pyridyl, pyrimidinyl, imidazolyl, pyrrolyl, pyrazolyl, furanyl, thienyl, oxazolyl, or isoxazolyl, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, sulfonamide, -CHO, halogen, oxo, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₇cycloalkyl, C₁-C₆alkoxy, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, (C₁-C₆alkoxy)C₁-C₆alkyl, (C₁-C₆alkoxy)C₁-C₆alkoxy, C₁-C₆alkylthio, mono- and di-(C₁-C₆alkyl)amino, amino(C₁-C₆alkyl), mono- and di-(C₁-C₆alkyl)amino(C₁-C₆alkyl), and C₂-C₆alkanoyl

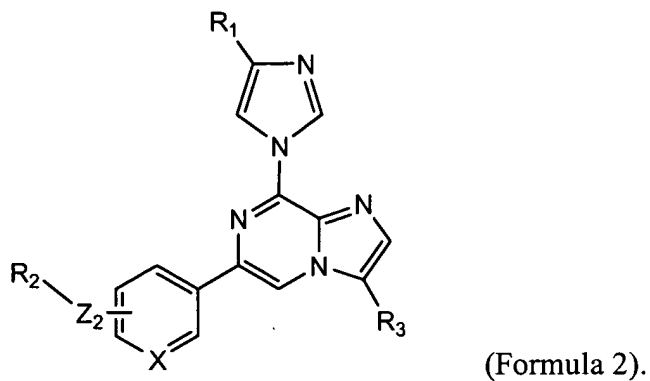
6. A compound or salt according to Claim 5 wherein

W is phenyl, pyridyl, pyrimidinyl, imidazolyl, pyrrolyl, pyrazolyl, furanyl, thienyl, oxazolyl, or isoxazolyl, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, halogen, oxo, C₁-C₄alkyl, C₁-C₄alkoxy, C₁-C₂haloalkyl, C₁-C₂haloalkoxy, and mono- and di-(C₁-C₄alkyl)amino.

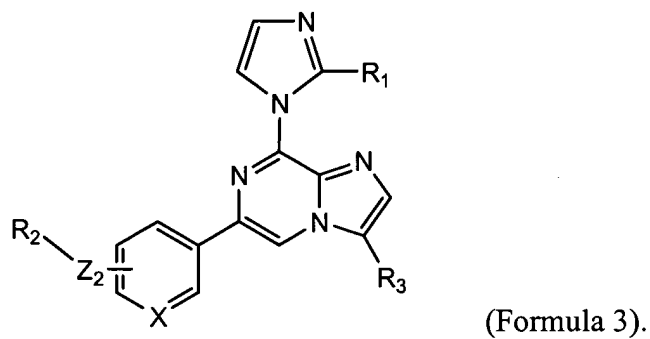
7. A compound or salt according to Claim 6, wherein

W is imidazolyl, pyrrolyl, or pyrazolyl, each of which is substituted with 0 to 2 substituents independently chosen from hydroxy, cyano, halogen, oxo, C₁-C₄alkyl, C₁-C₄alkoxy, trifluoromethyl, and trifluoromethoxy.

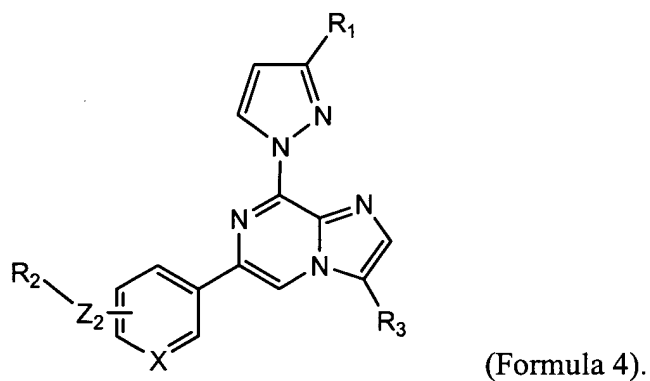
8. A compound or salt according to any one of Claims 1 to 4 of Formula 2



9. A compound or salt according to any one of Claims 1 to 4 of Formula 3

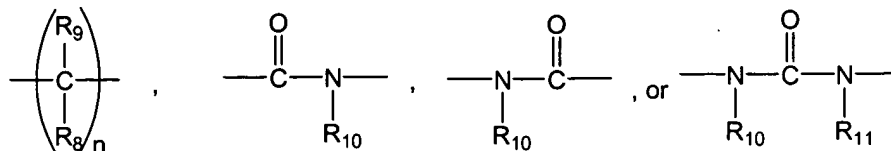


10. A compound or salt according to any one of Claims 1 to 4 of Formula 4



11. A compound or salt according to any one of Claims 1 to 10, wherein X is N.
12. A compound or salt according to any one of Claims 1 to 10, wherein X is CH.

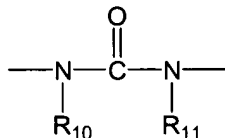
13. A compound or salt according to any one of Claims 1 to 12 wherein Z_2 is



wherein

R_8 and R_9 are independently hydrogen or C_1 - C_6 alkyl; and n is 0, 1, or 2; and R_{10} and R_{11} are independently hydrogen, C_1 - C_6 alkyl, or phenyl.

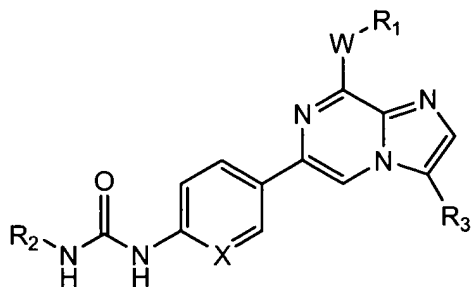
14. A compound or salt according to Claim 13, wherein Z_2 is



wherein, R_{10} and R_{11} are independently hydrogen, methyl or ethyl.

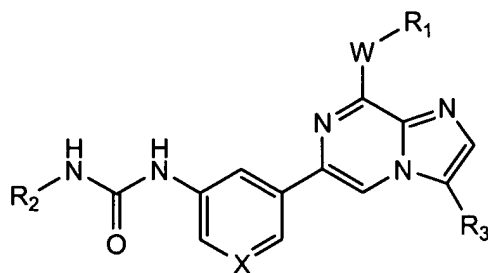
15. A compound or salt according to Claim 14 wherein R_{10} and R_{11} are both hydrogen.

16. A compound or salt according to any one of Claims 1 to 15 of Formula 5



(Formula 5).

17. A compound or salt according to any one of Claims 1 to 15 of Formula 6



(Formula 6).

18. A compound or salt according to any one of Claims 1 to 17 wherein

R₂ is phenyl, pyridyl, pyrimidinyl, pyrazinyl, imidazolyl, pyrrolyl, furanyl, thienyl, oxazolyl, or isoxazolyl, each of which may be either directly attached or bound via a C₁-C₂alkyl linker, and each of which is substituted with 0 to 3 substituents independently chosen from:

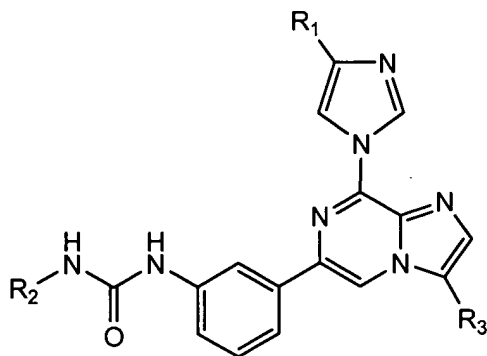
- (i) hydroxy, halogen, nitro, cyano, amino, sulfonamide, -CHO, C₁-C₆haloalkyl, and C₁-C₆haloalkoxy, and
- (ii) C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₇cycloalkyl, C₁-C₆alkoxy, (C₁-C₆alkoxy)C₁-C₆alkyl, (C₁-C₆alkoxy)C₁-C₆alkoxy, C₁-C₆alkylthio, mono- and di-(C₁-C₆alkyl)amino, amino(C₁-C₆alkyl), mono- and di-(C₁-C₆alkyl)amino(C₁-C₆alkyl), C₂-C₆alkanoyl, and heterocycloalkyl(C₀-C₂alkyl); each of which (ii) is substituted with 0 to 3 substituents independently chosen from halogen, hydroxy, amino, nitro, cyano, C₁-C₄alkoxy, C₃-C₇cycloalkyl, and mono- and di-(C₁-C₄alkyl)amino.

19. A compound or salt according to Claim 18, wherein

R₂ is phenyl(C₀-C₂alkyl), pyridyl(C₀-C₂alkyl), or pyrimidinyl(C₀-C₂alkyl), each of which is substituted with 0 to 3 substituents independently chosen from:

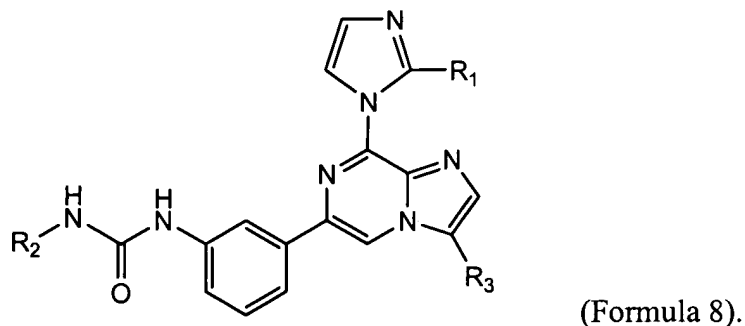
- (i) hydroxy, halogen, nitro, cyano, amino, C₁-C₂haloalkyl, and C₁-C₂haloalkoxy, and
- (ii) C₁-C₆alkyl, C₃-C₇cycloalkyl, C₁-C₆alkoxy, (C₁-C₆alkoxy)C₁-C₆alkyl, C₁-C₄alkylthio, mono- and di-(C₁-C₄alkyl)amino, mono- and di-(C₁-C₄alkyl)amino(C₁-C₄alkyl), and heterocycloalkyl(C₀-C₂alkyl); each of which (ii) is substituted with 0 to 3 substituents independently chosen from halogen, hydroxy, amino, nitro, cyano, C₁-C₄alkoxy, C₃-C₇cycloalkyl, and mono- and di-(C₁-C₄alkyl)amino.

20. A compound or salt according to Claim 19, wherein
 R_2 is phenyl or benzyl, each of which is substituted with 0 to 3 substituents independently chosen from halogen, hydroxy, amino, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, C_1 - C_4 alkylthio, C_1 - C_2 haloalkyl, and C_1 - C_2 haloalkoxy.
21. A compound or salt according to any one of Claims 1 to 20, wherein
 R_3 is hydrogen or C_1 - C_6 alkyl, or
 R_3 is C_3 - C_7 cycloalkyl, (C_3 - C_7 cycloalkyl)methyl, heterocycloalkyl, (heterocycloalkyl) C_1 - C_2 alkyl, phenyl, pyridyl, pyrimidinyl, pyrazinyl, imidazolyl, pyrrolyl, furanyl, thienyl, oxazolyl, or isoxazolyl, each of which is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, halogen, C_1 - C_6 alkyl, C_3 - C_7 cycloalkyl, C_1 - C_6 alkoxy, C_1 - C_2 haloalkyl, C_1 - C_2 haloalkoxy, and mono- and di-(C_1 - C_4 alkyl)amino; or
 R_3 is phenoxyphenyl, each of which phenyl rings is substituted with 0 to 3 substituents independently chosen from hydroxy, nitro, cyano, amino, halogen, C_1 - C_6 alkyl, C_3 - C_7 cycloalkyl, C_1 - C_6 alkoxy, C_1 - C_2 haloalkyl, C_1 - C_2 haloalkoxy, and mono- and di-(C_1 - C_4 alkyl)amino.
22. A compound or salt according to Claim 21, wherein
 R_3 is hydrogen, C_1 - C_6 alkyl, C_3 - C_7 cycloalkyl(C_0 - C_1 alkyl), phenyl, or phenoxyphenyl.
23. A compound or salt according to Claim 22, wherein R_3 is hydrogen or C_1 - C_4 alkyl.
24. A compound or salt according to Claim 1 of Formula 7

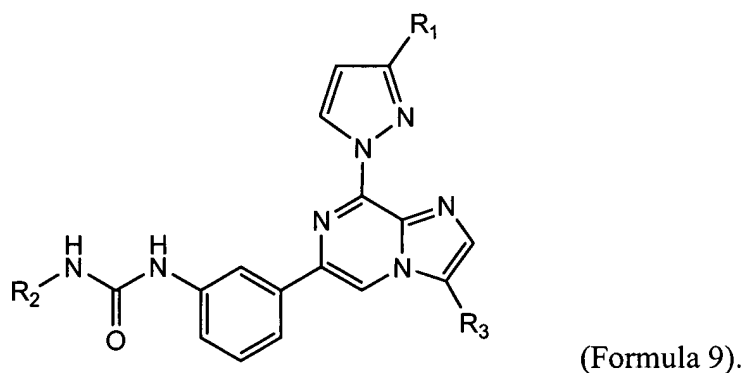


(Formula 7).

25. A compound or salt according to Claim 1 of Formula 8



26. A compound or salt according to Claim 1 of Formula 9



27. A compound or salt according to any one of Claims 24 to 26, wherein
 R_1 is 3-pyridyl or 4-pyridyl, each of which is substituted with 0 to 2 substituents independently chosen from fluoro, chloro, bromo, C_1 - C_2 alkyl, and C_1 - C_2 alkoxy;
 R_2 is phenyl or benzyl, each of which is substituted with 0 to 3 substituents independently chosen from: (i) hydroxy, halogen, amino, C_1 - C_2 haloalkyl, and C_1 - C_2 haloalkoxy, and
(ii) C_1 - C_6 alkyl, C_1 - C_6 alkoxy, mono- and di- $(C_1$ - C_4 alkyl)amino, mono- and di- $(C_1$ - C_4 alkyl)amino(C_1 - C_4 alkyl), piperazinyl(C_0 - C_1 alkyl), piperidinyl(C_0 - C_1 alkyl) and morpholinyl(C_0 - C_1 alkyl); each of which (ii) is substituted with 0 to 3 substituents independently chosen from halogen, hydroxy, amino, C_1 - C_2 alkoxy, and mono- and di- $(C_1$ - C_4 alkyl)amino; and
 R_3 is hydrogen or C_1 - C_4 alkyl.

28. A compound or form thereof according to Claim 1, wherein the compound is:

- 1-(2-Methoxy-5-trifluoromethyl-phenyl)-3-{3-[8-(2-pyridin-4-yl-imidazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea;
- 1-(4-Methoxy-3-trifluoromethyl-phenyl)-3-{3-[8-(2-pyridin-4-yl-imidazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea;
- 1-(2-Methoxy-5-trifluoromethyl-phenyl)-3-{3-[8-(2-pyridin-3-yl-imidazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea;
- 1-(5-Chloro-2-methoxy-phenyl)-3-{3-[8-(2-pyridin-4-yl-imidazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea;
- 1-(5-Fluoro-2-trifluoromethyl-phenyl)-3-{3-[8-(2-pyridin-4-yl-imidazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea;
- 1-(5-Chloro-2-trifluoromethyl-phenyl)-3-{3-[8-(2-pyridin-4-yl-imidazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea;
- 1-(5-Chloro-2,4-dimethoxy-phenyl)-3-{3-[8-(2-pyridin-4-yl-imidazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea;
- 1-(4-Methyl-3-trifluoromethyl-phenyl)-3-{3-[8-(2-pyridin-4-yl-imidazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea;
- 1-(4-Chloro-3-trifluoromethyl-phenyl)-3-{3-[8-(2-pyridin-4-yl-imidazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea; or
- 1-(2-Methoxy-5-trifluoromethyl-phenyl)-3-{3-[8-(3-pyridin-4-yl-pyrazol-1-yl)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-urea.

29. A compound or form thereof according to any one of Claims 1 to 28, wherein the compound exhibits a IC_{50} of 1 micromolar or less in a standard *in vitro* assay of EphB₄ kinase activity.

30. A compound or form thereof according to any one of Claims 1 to 28, wherein the compound exhibits a IC_{50} of 500 nanomolar or less in a standard *in vitro* assay of EphB₄ kinase activity.

31. A compound or form thereof according to any one of Claims 1 to 28, wherein the compound exhibits a IC_{50} of 100 nanomolar or less in a standard *in vitro* assay of EphB₄ kinase activity.

32. A pharmaceutical composition, comprising a compound or form thereof according to any one of Claims 1 to 31, together with at least one pharmaceutically acceptable carrier or excipient.

33. A pharmaceutical composition according to Claim 32, wherein the composition is formulated as an injectable fluid, an aerosol, a cream, a gel, a tablet, a pill, a capsule, a syrup, ophthalmic solution, or a transdermal patch.

34. A packaged pharmaceutical composition, comprising
(a) a pharmaceutical composition according to Claim 32 in a container; and
(b) instructions for using the composition to treat a patient suffering from a disease or disorder responsive to kinase activity modulation of one or more tyrosine kinase.

35. The packaged pharmaceutical composition of Claim 34 wherein the disease or disorder responsive to kinase activity modulation is cancer or a disease characterized by pathological angiogenesis.

36. The package pharmaceutical composition of Claim 34 wherein the disease characterized by pathological angiogenesis is a cancerous tumor, macular degeneration, or diabetic retinopathy.

37. A method of reducing medication error and enhancing therapeutic compliance of a patient being treated for a disease or disorder responsive to tyrosine kinase activity modulation, the method comprising providing a packaged pharmaceutical preparation according to Claim 34 wherein the instructions additionally include contraindication and adverse reaction information pertaining to the package pharmaceutical composition.

38. A method of modulating EphB₄ kinase activity, the method comprising contacting cells expressing EphB₄ kinase with a compound or form thereof according to any one of Claims 1 to 28 in an amount sufficient to detectably inhibit EphB₄ kinase activity *in vitro*.

39. A method of modulating VEGF-R2 activity, the method comprising contacting cells expressing VEGF-R2 with a compound or form thereof according to any one of Claims 1 to 28 in an amount sufficient to detectably inhibit VEGF-R2 activity *in vitro*.

40. A method of modulating c-Kit activity, the method comprising contacting cells expressing c-Kit with a compound or form thereof according to any one of Claims 1 to 28 in an amount sufficient to detectably inhibit c-Kit activity *in vitro*.

41. A method of modulating Tie-2 activity, the method comprising contacting cells expressing Tie-2 with a compound or form thereof according to any one of Claims 1 to 28 in an amount sufficient to detectably inhibit Tie-2 activity *in vitro*.

42. A method of modulating VEGF-R2, EphB₄, Tie-2, and c-Kit activity, the method comprising contacting cells expressing VEGF-R2, EphB₄, Tie-2, and c-Kit with a compound having a molecular weight less than 600 amu in an amount sufficient to detectably inhibit the activity of at least one of VEGF-R2, EphB₄, Tie-2, or c-Kit *in vitro*.

43. The method of Claim 42 wherein the compound is a heterocyclic compound.

44. The method of Claim 43 wherein the compound is a heterocyclic compound comprising a bicyclic heterocyclic group.

45. The method of Claim 43 wherein the compound is a compound of Claims 1 to 28 or form thereof.

46. A method of treating a patient having a disease or disorder responsive to kinase activity modulation comprising administering to the patient an effective amount of a compound according to any one of Claims 1 to 28.

47. The method of 46 wherein the patient is a human.

48. The method of Claim 46 wherein the patient is a cat or dog.

49. The method of Claim 46 wherein the disease or disorder responsive kinase activity modulation is cancer or a disease characterized by pathological angiogenesis.

50. The method of Claim 49 wherein the disease characterized by pathological angiogenesis is a cancerous tumor, macular degeneration, or diabetic retinopathy.

51. The method of Claim 46 wherein the compound or form is administered orally.

52. A method for determining the presence or absence of an angiogenic kinase in a sample comprising contacting the sample with a compound or form thereof according to any one of Claims 1 to 28 under conditions that permit binding of the compound or form to the angiogenic kinase, detecting a level of the compound or form bound to the angiogenic kinase, and therefrom determining the presence or absence of the angiogenic kinase.

53. The method of Claim 52 wherein the angiogenic kinase is Tie-2, VEGF-R2, or EphB₄.

54. The method of Claim 53 wherein the compound or form thereof is radiolabelled.

55. The method of Claim 53, which additionally comprises separating unbound compound from bound compound; and determining the amount of bound compound in the sample.

56. The method of claim 42 wherein the cells expressing VEGF-R2, EphB₄, Tie-2, and c-Kit with a compound are contacted with the compound having a molecular weight less than 600 amu in an amount sufficient to detectably inhibit the activity of VEGF-R2, EphB₄, Tie-2, and c-Kit *in vitro*.